

SAS:sas 09/28/07 771332.doc E-153-2002/1-US-03  
PATENT

Attorney Reference Number 4239-66899-01  
Application Number 10/666,022

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**In re application of:** Klinman et al.

**Application No.** 10/666,022

**Filed:** September 17, 2003

**Confirmation No.** 7954

**SUBMITTED VIA EFS  
OCTOBER 1, 2007**

**For:** METHOD OF TREATING AND  
PREVENTING INFECTIONS IN  
IMMUNOCOMPROMISED SUBJECTS  
WITH IMMUNOSTIMULATORY CPG  
OLIGONUCLEOTIDES

**Examiner:** Michelle S. Horning

**Art Unit:** 1645

**Attorney Reference No.** 4239-66899-01

SUBMITTED BY THE ELECTRONIC FILING SYSTEM  
COMMISSIONER FOR PATENTS

**DECLARATION UNDER 37 C.F.R. § 1.131**

We, Dennis Klinman and Daniela Verithelyi declare as follows:

1. We are the inventors of the above-identified application, claims the benefit of U.S. Provisional Application No. 60/411,944, filed September 18, 2002.
2. We have reviewed the Office action dated August 31, 2007. It is our understanding that claims 1-3, 7-8, 14-17, 21, 23 and 25-27 are rejected as allegedly being anticipated under 35 U.S.C. § 102(c) as allegedly being anticipated by U.S. Patent Application No. 10/502, 085 (Jiang et al.), which has an effective filing date of February 4, 2002.
3. We conceived of, and reduced to practice, a method for increasing an immune response to an opportunistic infection in an immunocompromised subject by administering a therapeutically effective amount of a D ODN substantially prior to February 4, 2002 in the United States of America (a World Trade Organization (WTO) country).

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4. To assess whether the immune response to CpG ODN generated in immunosuppressed HIV patients would suffice to generate an immunoprotective response *in vivo*, rhesus macaques that had been infected with SIV strain mac239 a year before the start of the study (Viral load range:  $0.3-28 \times 10^6$  copies/ml) were utilized. Monkeys were treated *i.d.* with D ODN ("D"), K ODN ("K"), control ODN ("C") or saline ("S") 3 days before and 3 days after an intra-dermal challenge with  $10^7$  viable metacyclic promastigotes of *L. major* (WHOM/IR/-/173), a strain of *Leishmania* that frequently infects HIV patients. The lesion size, which reflects the severity of infection (Amaral, *et al.*, 1996, *Exp. Parasitol.* 82:34), was measured weekly. The protocol for this experiment is shown in Exhibit A. Control monkeys developed a typical *in situ* inflammatory lesion characterized by erythema, induration, and ulceration. As shown in Exhibit B, monkeys treated with D ODN had smaller lesions than control or saline treated monkeys. This difference was statistically significant. All of the work and the analyses were performed prior to February 4, 2002.


5. All statements made herein and of our own knowledge are true and all statements made on information are believed to be true; and further, these statements were made with the knowledge that willful false statements and like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements made may jeopardize the validity of the application or any patent issuing thereon.

Date

Sept 28, 2007

  
Dennis Klinman

Date

  
Daniela Veritheyli

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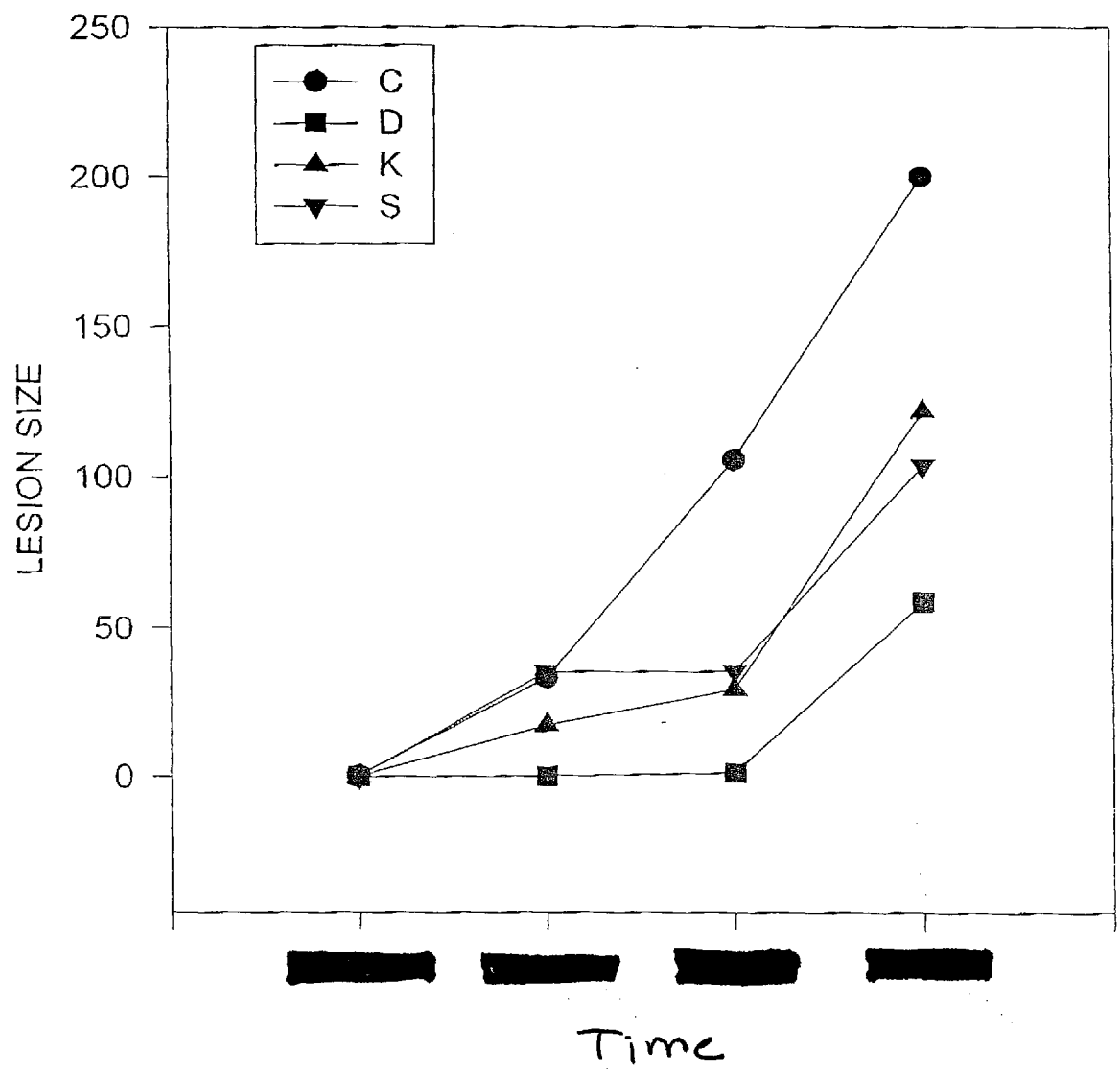
Date \_\_\_\_\_

Dennis Klinman

Date 9-28-2007

Daniela Vertueyt

Lesion size in SIV infected Rhesus monkeys infected with L.Major



**CpG as protection from *Leishmania* infection in SIV Rhesus Monkeys**

Day	Wk	Date	Activity	Tubes		Comment
				P	R	
-3		██████	Inject CpG 500ug id Bleed	1	1	Prebleed for Screen ODN in vitro Ag-specific prol/IFN $\gamma$
0	0	██████	Injects <i>Leishmania</i> id	1		
3		██████	Inject CpG 500 ug id	1		
7	1	██████	Measure lesions	1		
21	3	██████	Measure lesions	1		
28	4	██████	Measure lesions	1		Ag-specific prol/IFN $\gamma$
35	5	██████	Measure lesions	1		
42	6	██████	Measure lesions	1		
49	7	██████	Measure lesions	1		
56	8	██████	Measure lesions	1		
63	9	██████	Measure lesions	1		

P= Purple tube (3 ml)

R= Red Tube (20 ml)